

a.) Amendment to the Specification:

Please amend the paragraph at page 14, lines 11-28 to read as follows.

Examples of the heterocyclic group moiety of the heterocyclic group and heterocyclic alkyl include groups described in the above definition of the aromatic heterocyclic group and also alicyclic heterocyclic groups. Examples of the alicyclic heterocyclic group include 5- or 6-membered monocyclic alicyclic heterocyclic groups containing at least one atom selected from a nitrogen atom, an oxygen atom and a sulfur atom, and bicyclic or tricyclic condensed-ring alicyclic heterocyclic groups containing at least one atom selected from a nitrogen atom, an oxygen atom and a sulfur atom in which 3- to 8-membered rings are condensed, such as pyrrolidinyl, piperidino, piperazinyl, ~~piperazinyl~~, morpholino, morpholinyl, thiomorpholino, thiomorpholinyl, homopiperidino, homopiperazinyl, ~~homopiperazinyl~~, tetrahydropyridinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, tetrahydrofuranyl, tetrahydropyranyl, dihydrobenzofuranyl, oxopiperazinyl and 2-oxopyrrolidinyl.

Please amend the paragraph at page 26, lines 7-13 to read as follows.

Compound (Ic), i.e. Compound (I) in which R³ and R⁵ each are a hydrogen atom, can also be produced from Compound (Ib), i.e. Compound (I) in which R³ is R^{3a} (wherein R^{3a} has the same meaning as the above-described R³ except a hydrogen atom is excluded) and R⁵ is R^{5a} (wherein R^{5a} has the same meaning as the above-described R⁵ except a hydrogen atom is excluded), according to the following step.

Please amend the paragraph at page 27, lines 13-20 to read as follows.

Compound (Ic) can also be obtained by treating Compound (Ib-i) with palladium (II) acetate in the presence or absence of a ligand such as triphenylphosphine, or with a palladium complex such as tetrakis ~~triphenylphosphine~~ palladium (II), ~~(triphenylphosphine)~~ palladium (0), selenium dioxide or the like, in an organic acid such as acetic acid or formic acid or in a mixed solvent of an organic acid and tetrahydrofuran.

Please amend the paragraph at page 46, lines 6-12 to read as follows.

(1) Human N-terminal recombinant Hsp90 protein (region of amino acids 9 to 236) prepared according to the method described in "Cell", 1997, Vol. 89, p. 239-250 was diluted to 1 μ g/mL with Tris-buffered saline (TBS, pH 7.5) and added to each well of a 96-well ELISA assay plate (Greiner) in an amount of 70 μ L/well. The plate was incubated overnight at 4°C to obtain the solid phase coated with the Hsp90 protein.

Please amend the paragraph at page 46, lines 21-32 to read as follows.

(4) A test compound having the highest concentration of 0.1 mmol/L was diluted with TBST to prepare eight $\sqrt{10}$ -fold serial dilutions in separate vials. Each of these test compound solutions was added, in an amount of 10 μ L/well, to the assay plate containing TBST (90 μ L/well) previously added thereto, and the plate was allowed to stand at 24°C for 1 hour. In this assay, a positive control using dimethyl sulfoxide (final concentration: 0.1 μ L/well) (final volume: 0.1 μ L/well) and a negative control using Radicicol (final concentration: 0.29 μ mol/L) were subjected to the same procedure as the

test compound, and these controls were on the same plate which was placed the test compound thereon.

Please amend the paragraph at page 57, lines 2-21 to read as follows.

2-[3,5-Bis(methoxymethoxy)-2-phenylphenyl]ethanol (1.2 g, 3.7 mmol) obtained in Example 3, Step 3 was dissolved in N,N-dimethylformamide (15 mL), and a 60% sodium hydride dispersion in mineral oil (0.30 g, 7.5 mmol) was added thereto in an atmosphere of nitrogen, followed by stirring at 4°C for 4 minutes. After methyl iodide (0.70 mL, 11 mmol) was added dropwise to the reaction mixture, the mixture was stirred at 4°C for 1 hour, followed by further stirring for 48 hours, while the temperature of the mixture was raised to room temperature. To the reaction mixture was added water (10 mL) and a saturated aqueous solution of ammonium chloride (20 mL), and the mixture was extracted with ethyl acetate (0.10 L). The organic layer was washed with water (0.10 L) and dried over anhydrous sodium sulfate, followed by concentration under reduced pressure. The resulting residue was purified by silica gel column chromatography (ethyl acetate/hexane = 1/9-1/2) to obtain 3,5-bis(methoxymethoxy)-1-(2-methoxyethyl)-2-phenylbenzene (1.1 g, 91%).

Please amend the paragraph at page 75, lines 6-13 to read as follows.

In a manner similar to that in Example 10, Step 2, Compound 13 (40 mg, 30%) was obtained from 2-ethyl-3,5-dihydroxy-6-(4-methoxybenzoyl)phenylacetic acid (0.10 g, 0.30 mmol) obtained in Example 10, Step 1, using N-hydroxysuccinimide (~~0.11 g~~,

0.96 mmol, (0.11 g, 0.96 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.12 g, 0.61 mmol), diethanolamine (0.087 mL, 0.91 mmol) and N,N-dimethylformamide (1.0 mL).

Please amend the paragraph starting at page 76, line 29 and ending at page 77, line 5 to read as follows.

Methyl 3,5-diallyloxy-2-iodo-6-(4-methoxybenzoyl)-phenylacetate (80 mg, 0.15 mmol) obtained in Example 15, Step 2 was dissolved in 1,4-dioxane (1.0 mL), and selenium dioxide (36 mg, 0.34 mmol) and acetic acid (~~0.028 mL, 0.46 mL~~ 0.028 mL, 0.46 mmol) were added thereto, followed by stirring at 75°C for half a day. The reaction mixture was poured into a saturated aqueous solution of sodium hydrogencarbonate, followed by extraction with chloroform. The organic layer was dried over anhydrous sodium sulfate and then concentrated under reduced pressure. The resulting residue was purified by preparative thin layer chromatography (chloroform/methanol = 9/1) to obtain Compound 15 (1.2 mg, 8.2%).

Please amend the paragraph at page 78, lines 20-32 to read as follows.

Methyl 3,5-diallyloxy-2-(4-methoxybenzoyl)phenyl-acetate (100 mg, 0.25 mmol) obtained in Example 15, Step 1 was dissolved in dichloromethane (10 mL). After the solution was cooled to -78°C, a 1.0 mol/L solution of boron tribromide in hexane (0.50 mL, 0.5 mmol) was added thereto, followed by stirring at -78°C for 30 minutes. To the reaction mixture were successively added methanol and a saturated aqueous solution of sodium hydrogencarbonate, followed by extraction with chloroform. The organic layer

was dried over anhydrous sodium sulfate and then concentrated under reduced pressure.

The resulting residue was purified by preparative thin layer chromatography

(chloroform/methanol = 20/1) to obtain Compound 18 (54 mg, 61%).

Please amend the paragraph starting at page 94, line 31 and ending at page 95, line 2 to read as follows.

In a manner similar to that in Example 10, Step 2, Compound 41 (49 mg, 34%) was obtained from ~~2-(3,4-dimethoxybenzoyl-6-ethyl-3,5-dihydroxy)phenylacetic acid~~ 2-(3,4-dimethoxybenzoyl)-6-ethyl-3,5-dihydroxyphenylacetic acid (0.10 g, 0.29 mmol) obtained in Example 40, Step 1, using 1-hydroxybenzotriazole hydrate (0.11 g, 0.71 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.13 g, 0.66 mmol), 1-phenylpiperazine (0.13 mL, 0.86 mmol) and N,N-dimethylformamide (1.0 mL).

Please amend the paragraphs at page 112, lines 20-24 to read as follows.

Synthesis of 6-[2-(2,3-dihydroxypropyloxy)ethyl]-5-ethyl-2,4-dihydroxyphenyl=4-methoxy-3-(3-methoxyphenyl)phenyl=ketone (Compound 59)

(Step 1)

Please amend the paragraph at page 126, lines 22-30 to read as follows.

In a manner similar to that in Example 59, Step 3, 4,6-diallyloxy-3-ethyl-2-[2-(2-hydroxyethoxy)ethyl]phenyl=3-furyl=ketone (35 mg, 23%) was obtained from ~~2-[2-(3,5-diallyloxy-2-ethylphenyl)ethoxy]ethanol~~ 2-[2-(3,5-diallyloxy-2-

ethylphenyl)ethoxy]ethanol (0.11 g, 0.37 mmol) obtained in Example 59, Step 2, using trifluoroacetic acid (4.0 mL), 3-furancarboxylic acid (90 mg, 0.80 mmol) and trifluoroacetic anhydride (1.0 mL, 0.71 mmol), and using acetonitrile (2.0 mL) and a 2 mol/L aqueous solution of sodium hydroxide (2.0 mL).

Please amend the paragraph at page 131, lines 28-36 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 78 (88 mg, 60%) was obtained from 2-benzoyl-6-ethyl-3,5-dihydroxyphenylacetic acid (0.11 g, 0.37 mmol) obtained in Example 74, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.16 g, 0.84 mol), (0.16 g, 0.84 mmol), 4-piperidineethanol (0.17 g, 1.5 mmol), 1-hydroxybenzotriazole hydrate (0.14 g, 0.91 mmol) and N,N-dimethylformamide (1.0 mL). In this case, crystallization was carried out with ethyl acetate.

Please amend the paragraph at page 133, lines 12-21 to read as follows.

In a manner similar to that in Example 10, Step 2, 2-[2-ethyl-3,5-diallyloxy-6-(4-hydroxybenzoyl)phenyl]-N-(2-hydroxyethyl)-N-(2-methoxyethyl)acetamide 2-[2-ethyl-3,5-diallyloxy-6-(3-hydroxybenzoyl)phenyl]-N-(2-hydroxyethyl)-N-(2-methoxyethyl)acetamide (430 mg, 74%) was obtained from 3,5-diallyloxy-2-ethyl-6-(3-hydroxybenzoyl)phenylacetic acid (470 mg, 1.2 mmol) obtained in Example 78, Step 2, using 1-hydroxybenzotriazole hydrate (220 mg, 1.4 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (270 mg, 1.4 mmol), 2-(2-methoxyethylamino)ethanol

(170 mg, 1.4 mmol) obtained in Reference Example 1 and N,N-dimethylformamide (10 mL).

Please amend the paragraph at page 136, lines 23-29 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 82 (110 mg, 72%) was obtained from 2-ethyl-6-(4-fluorobenzoyl)-3,5-dihydroxyphenylacetic acid (0.11 g, 0.33 mmol) obtained in Example 49, Step 3, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (0.12 g, 0.76 mol), (0.12 g, 0.76 mmol), 1-phenylpiperazin-2-one hydrochloride (0.28 g, 1.3 mmol) and N,N-dimethylformamide (1.0 mL).

Please amend the paragraph at page 138, lines 6-15 to read as follows.

In a manner similar to that in Example 10, Step 2, ~~2-[2-ethyl-3,5-allyloxy-6-(3-hydroxy-4-methoxybenzoyl)-phenyl]-N,N-bis(2-hydroxyethyl)acetamide~~ 2-[2-ethyl-3,5-diallyloxy-6-(3-hydroxy-4-methoxybenzoyl)-phenyl]-N,N-bis(2-hydroxyethyl)acetamide (85 mg, 35%) was obtained from 3,5-diallyloxy-2-ethyl-6-(3-hydroxy-4-methoxybenzoyl)phenylacetic acid (200 mg, 0.47 mmol) obtained in Example 82, Step 2, using 1-hydroxybenzotriazole hydrate (150 mg, 0.98 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (180 mg, 0.94 mmol), diethanolamine (150 mg, 1.4 mmol) and N,N-dimethylformamide (4 mL).

Please amend the paragraph at page 138, lines 25-31 to read as follows.

In a manner similar to that in Example 7, Step 1, Compound 83 (47 mg, 66%) was obtained from ~~2-[2-ethyl-3,5-allyloxy-6-(3-hydroxy-4-methoxybenzoyl)phenyl]-N,N-bis(2-hydroxyethyl)acetamide~~ 2-[2-ethyl-3,5-diallyloxy-6-(3-hydroxy-4-methoxybenzoyl)phenyl]-N,N-bis(2-hydroxyethyl)acetamide (85 mg, 0.17 mmol) obtained in Example 82, Step 3, using ammonium formate (50 mg, 0.79 mmol), bis(triphenylphosphine)palladium (II) dichloride (10 mg, 0.14 mmol) and 1,4-dioxane (3 mL).

Please amend the paragraph at page 140, lines 29-36 to read as follows.

In a manner similar to that in Example 7, Step 1, methyl 2-ethyl-6-(3-fluoro-4-methoxybenzoyl)-3,5-dihydroxy-phenylacetate (1.0 g, 95%) was obtained from ~~methyl 3,5-diallyloxy-2-ethyl-6-(3-fluoro-4-methoxyhydroxybenzoyl)-phenylacetate~~ 3,5-diallyloxy-2-ethyl-6-(3-fluoro-4-methoxybenzoyl)-phenylacetate (1.3 g, 2.9 mmol) obtained in Example 84, Step 1, using ammonium formate (1.0 g, 16 mmol), bis(triphenylphosphine)palladium (II) dichloride (0.10 g, 0.14 mmol) and 1,4-dioxane (20 mL).

Please amend the paragraph at page 152, lines 21-27 to read as follows.

In a manner similar to that in Example 10, Step 1, ~~3,5-diallyloxy-2-ethyl-6-(3-methylthiobenzoyl)phenylacetate~~ 3,5-diallyloxy-2-ethyl-6-(3-methylsulfanybenzoyl)phenylacetic acid was obtained from methyl 3,5-diallyloxy-2-ethyl-

6-(3-methylsulfanylbenzoyl)phenylacetate (200 mg, 0.46 mmol) obtained in Example 94, Step 1, using a 2 mol/L aqueous solution of sodium hydroxide (5 mL) and tetrahydrofuran (5 mL).

Please amend the paragraph at page 156, lines 11-18 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 98 (14 mg, 7.4%) was obtained from 2-ethyl-3,5-dihydroxy-6-(4-methoxybenzoyl)phenylacetic acid (0.11 g, 0.33 mmol) obtained in Example 10, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (~~0.15 g, 0.76 mol~~, (0.15 g, 0.76 mmol), (R)-(-)-2-pyrrolidinemethanol (0.13 mL, 1.3 mmol) and N,N-dimethylformamide (1.0 mL). In this case, crystallization was carried out with ethyl acetate.

Please amend the paragraph starting at page 156, line 30 and ending at page 157, line 1 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 99 (0.013 g, 17%) was obtained from 2-(3,4-dimethoxybenzoyl)-6-ethyl-3,5-dihydroxyphenylacetic acid (0.059 g, 0.16 mmol) obtained in Example 40, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (~~0.064 g, 0.33 mol~~, (0.064 g, 0.33 mmol), 3-(2-hydroxyethyl-amino)propanol (0.040 g, 0.34 mmol) and N,N-dimethylformamide (0.50 mL).

Please amend the paragraph at page 170, lines 29-31 to read as follows.

Synthesis of 2-{2-ethyl-3,5-dihydroxy-6-[3-methoxy-4-(2-morpholinoethoxy)benzoyl]phenyl}-N-(2-hydroxyethyl)-N-(2-methoxyethyl)acetamide 2-{2-ethyl-3,5-dihydroxy-6-[3-methoxy-4-(2-morpholinoethoxy)benzoyl]phenyl}-N-(2-hydroxyethyl)-N-(2-methoxyethyl)acetamide (Compound 110)

Please amend the paragraph at page 171, lines 16-22 to read as follows.

In a manner similar to that in Example 10, Step 1, 3,5-diallyloxy-2-ethyl-6-{3-methoxy-4-(2-morpholino-ethoxy)benzoyl}phenylacetic acid was obtained from methyl ~~3,5-diallyloxy-2-ethyl-6-[3-methoxy-4-(2-morpholinoethoxy)benzoyl]~~ ~~3,5-diallyloxy-2-ethyl-6-[3-methoxy-4-(2-morpholinoethoxy)benzoyl]~~ phenylacetate (300 mg, 0.54 mmol) obtained in Example 109, Step 1, using a 2 mol/L aqueous solution of sodium hydroxide (5 mL) and tetrahydrofuran (5 mL).

Please amend the paragraph starting at page 171, line 33 and ending at page 172, line 3 to read as follows.

In a manner similar to that in Example 7, Step 1, Compound 110 (160 mg, 52% in 3 steps) was obtained from ~~3,5-diallyloxy-2-ethyl-6-[3-methoxy-4-(2-morpholinoethoxy)benzoyl]phenyl}-N-(2-hydroxyethyl)-N-(2-methoxyethyl)acetamide from 2-{3,5-diallyloxy-2-ethyl-6-[3-methoxy-4-(2-morpholinoethoxy)benzoyl]phenyl}-N-(2-hydroxyethyl)-N-(2-methoxyethyl)acetamide obtained above, using ammonium formate (150 mg, 2.4 mmol), bis(triphenylphosphine)palladium (II) dichloride (20 mg, 0.029 mmol) and 1,4-dioxane (5 mL).~~

Please amend the paragraph at page 172, lines 18-24 to read as follows.

In a manner similar to that in Example 10, Step 1, 3,5-diallyloxy-2-ethyl-6-(4-methoxybenzoyl)phenylacetic acid (2.2 g, 80%) was obtained from methyl 3,5-diallyloxy-2-ethyl-(4-methoxybenzoyl)phenylacetate (2.8 g, 6.6 mmol) obtained in Example 6, Example 8, Step 1, using a 2 mol/L aqueous solution of sodium hydroxide (10 mL) and acetonitrile (10 mL).

Please amend the paragraph starting at page 172, line 34 and ending at page 173, line 20 to read as follows.

3,5-Diallyloxy-2-ethyl-6-(4-methoxybenzoyl)-phenylacetic acid (0.22 g, 0.53 mmol) obtained in Example 110, Step 1 was dissolved in N,N-dimethylformamide (2.0 mL). To the solution were added 1-hydroxybenzotriazole hydrate (70 mg, 0.46 mmol), N-methylmorpholine (0.20 mL, 1.8 mmol), 2-(2-morpholinoethylamino)ethanol (0.18 mL, 1.1 mmol) obtained in Reference Example 4 and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (~~0.12 g, 0.63 mol~~, 0.12 g, 0.63 mmol), followed by stirring at room temperature for 15 hours. The reaction mixture was concentrated under reduced pressure, and the resulting residue was dissolved in ethyl acetate. To the resulting solution was added a saturated aqueous solution of sodium chloride for liquid separation. The organic layer was dried over anhydrous sodium sulfate and then concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography [amino type chemically bonded silica gel: Chromatorex (trademark) NH, product of Fuji Silijsia Chemical Ltd., ethyl acetate-methanol/ethyl acetate = 1/19] to obtain a quantitative

yield of ~~3,5-diallyloxy-2-ethyl-6-(4-methoxybenzoyl)phenyl]-N-(2-hydroxyethyl)-N-(2-morpholinoethyl)acetamide~~ 2-3,5-diallyloxy-2-ethyl-6-(4-methoxybenzoyl)phenyl]-N-(2-hydroxyethyl)-N-(2-morpholinoethyl)acetamide.

Please amend the paragraph at page 178, lines 6-13 to read as follows.

In a manner similar to that in Example 110, Step 3, Compound 114 (15 mg, 8.6%) was obtained from ~~2-[3,5-allyloxy-2-(3,4-dimethoxybenzoyl)-6-ethylphenyl]-N-(2-diethylaminoethyl)-N-(2-hydroxyethyl)acetamide~~ 2-[3,5-diallyloxy-2-(3,4-dimethoxybenzoyl)-6-ethylphenyl]-N-(2-diethylaminoethyl)-N-(2-hydroxyethyl)acetamide (0.20 g, 0.34 mmol) obtained in Example 113, Step 1, using ammonium formate (86 mg, 1.4 mmol), bis(triphenylphosphine)palladium (II) dichloride (7.2 mg, 0.010 mmol) and 1,4-dioxane (1.5 mL).

Please amend the paragraph at page 179, lines 12-19 to read as follows.

In a manner similar to that in Example 110, Step 3, Compound 115 (0.22 g, 78%) was obtained from ~~2-[3,5-diallyloxy-2-(3,4-dimethoxybenzoyl)-6-ethylphenyl]-N-(2-hydroxyethyl)-N-[2-(4-morpholino)ethyl]acetamide~~ 2-[3,5-diallyloxy-2-(3,4-dimethoxybenzoyl)-6-ethylphenyl]-N-(2-hydroxyethyl)-N-(2-morpholinoethyl)acetamide (0.33 g, 0.55 mmol) obtained in Example 114, Step 1, using ammonium formate (0.14 g, 2.2 mmol), bis(triphenylphosphine)palladium (II) dichloride (12 mg, 0.017 mmol) and 1,4-dioxane (1.5 mL).

Please amend the paragraph at page 181, lines 9-18 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 117 (0.26 g, 62%) was obtained from 2-ethyl-3,5-dihydroxy-6-(4-methoxybenzoyl)phenylacetic acid (0.31 g, 0.93 mmol) obtained in Example 10, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (~~0.23 g, 1.22 mol~~, (0.23 g, 1.22 mmol), 3-(2-methoxyethylamino)propanol (0.19 g, 1.4 mmol) obtained in Reference Example 2 and N,N-dimethylformamide (3.0 mL). In this case, crystallization was carried out with a mixed solvent of ethyl acetate and acetonitrile.

Please amend the paragraph starting at page 181, line 34 and ending at page 182, line 7 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 118 (0.17 g, 42%) was obtained from 2-ethyl-3,5-dihydroxy-6-(4-methoxybenzoyl)phenylacetic acid (0.30 g, 0.92 mmol) obtained in Example 10, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (~~0.23 g, 1.20 mol~~, (0.23 g, 1.20 mmol), 2-(3-methoxypropylamino)ethanol (0.19 g, 1.4 mmol) obtained in Reference Example 3 and N,N-dimethylformamide (3.0 mL). In this case, crystallization was carried out with a mixed solvent of ethyl acetate and acetonitrile.

Please amend the paragraph at page 182, lines 26-33 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 119 (0.23 g, 54%) was obtained from 2-(3,4-dimethoxybenzoyl)-6-ethyl-3,5-dihydroxyphenylacetic acid (0.31 g, 0.87 mmol) obtained in Example 40, Step 1, using 1-(3-

dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.23 g, 1.2 mol), (0.23 g, 1.2 mmol), 3-(2-methoxyethyl-amino)propanol (0.19 g, 1.4 mmol) obtained in Reference Example 2 and N,N-dimethylformamide (3.0 mL). In this case, crystallization was carried out with a mixed solvent of ethyl acetate and methanol.

Please amend the paragraph at page 183, lines 13-22 to read as follows.

In a manner similar to that in Example 74, Step 2, Compound 120 (0.15 g, 37%) was obtained from 2-(3,4-dimethoxybenzoyl)-6-ethyl-3,5-dihydroxyphenylacetic acid (0.31 g, 0.87 mmol) obtained in Example 40, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.23 g, 1.2 mol), (0.23 g, 1.2 mmol), -(3-methoxypropylamino)ethanol (0.19 g, 1.4 mmol) obtained in Reference Example 3 and N,N-dimethylformamide (3.0 mL). In this case, crystallization was carried out with a mixed solvent of ethyl acetate and methanol.

Please amend the paragraph at page 184, lines 3-9 to read as follows.

In a manner similar to that in Example 5, Step 4, methyl 3,5-diallyloxy-6-(4-ethoxybenzoyl)-2-ethyl phenylacetate 3,5-diallyloxy-2-(4-ethoxybenzoyl)-6-ethyl phenylacetate (1.1 g, 73%) was obtained from methyl 3,5-diallyloxy-2-ethylphenylacetate (1.0 g, 3.5 mmol) obtained in Example 5, Step 3, using 3-ethoxybenzoic acid (0.86 g, 5.2 mmol), trifluoroacetic anhydride (0.73 mL, 5.2 mmol) and trifluoroacetic acid (20 mL).

Please amend the paragraphs at page 188, lines 4-7, to read as follows.

Synthesis of 2-[2-ethyl-3,5-dihydroxy-6-(4-isopropoxy-benzoyl)phenyl]-N-(2-hydroxyethyl)-N-(2-methoxyethyl)-acetamide (Compound 124)

(Step 1)

Please amend the paragraphs starting at page 199, line 28 and ending at page 200, line 6 to read as follows.

Synthesis of 2-[2-(4-ethoxybenzoyl)-6-ethyl-3,5-dihydroxyphenyl]-N-(2-methoxyethyl)-N-(2-morpholinoethyl)-acetamide (Compound 133)

(Step 1)

In a manner similar to that in Example 10, Step 2, 2-[3,5-diallyloxy-2-(4-ethoxybenzoyl)-6-ethylphenyl]-N-(2-methoxyethyl)-N-(2-morpholinoethyl)acetamide was obtained from ~~3,5-diallyloxy-2-ethyl-6-(4-ethoxybenzoyl)-phenylacetic~~ 3,5-diallyloxy-2-(4-ethoxybenzoyl)-6-ethylphenylacetic acid (340 mg, 0.80 mmol) obtained in Example 120, Step 2, using 1-hydroxybenzotriazole hydrate (190 mg, 1.2 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (230 mg, 1.2 mmol), N-methylmorpholine (0.27 mL, 2.6 mmol), N-(2-methoxyethyl)-2-morpholinoethylamine (300 mg, 1.6 mmol) obtained in Reference Example 5 and N,N-dimethylformamide (8 mL).

Please amend the paragraph at page 200, lines 22-25 to read as follows.

Synthesis of 2-[2-ethyl-3,5-dihydroxy-6-(4-isopropoxy-benzoyl)phenyl]-N-(2-methoxyethyl)-N-(2-morpholinoethyl)-acetamide (Compound 134)

(Step 1)

Please amend the paragraph at page 201, lines 20-25 to read as follows.

In a manner similar to that in Example 88, Step 1, methyl 3,5-dihydroxy-2-(4-methoxybenzoyl)phenylacetate (2.9 g, 82%) was obtained from methyl 3,5-dihydrophenylacetate 3,5-dihydroxyphenylacetate (2.0 g, 11 mmol), using 4-methoxybenzoic acid (2.0 g, 13 mmol) and boron trifluoride diethyl etherate (40 mL).

Please amend the paragraph at page 208, lines 10-16 to read as follows.

In a manner similar to that in Example 10, Step 1, 3,5-diallyloxy-2-[3,4-bis(2-methoxyethoxy)benzoyl]-6-ethylphenylacetic acid (0.46 g, 95%) was obtained from methyl 3,5-diallyloxy-2-ethyl-6-[3,4-bis(2-methoxyethoxy)-benzoyl]phenylacetate 3,5-diallyloxy-2-[3,4-bis(2-methoxyethoxy)-benzoyl]-6-ethylphenylacetate (0.48 g, 0.89 mmol) obtained in Example 136, Step 2, using a 2 mol/L aqueous solution of sodium hydroxide (5 mL) and acetonitrile (10 mL).

Please amend the paragraphs at page 209, lines 17-20 to read as follows.

Synthesis of 2-{2-[3,4-bis(2-methoxyethoxy)benzoyl]-3,5-dihydroxy-6-ethylphenyl}-N-(2-hydroxyethyl)-N-(2-methoxy-ethyl)acetamide (Compound 138)

(Step 1)

Please amend the paragraphs at page 210, lines 11-14 to read as follows.

Synthesis of 2-{2-ethyl-3,5-dihydroxy-6-[3-methoxy-4-(2-morpholinoethoxy)benzoyl]phenyl}-N,N-bis(2-methoxyethyl)-acetamide hydrochloride (Compound 139)

(Step 1)

Please amend the paragraph at page 211, lines 3-12 to read as follows.

In a manner similar to that in Example 110, Step 2, Compound 140 (0.089 g, 61%) was obtained from 2-ethyl-3,5-dihydroxy-6-(4-methoxybenzoyl)phenylacetic acid (0.10 g, 0.31 mmol) obtained in Example 10, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.090 g, 0.47 mmol), (0.090 g, 0.47 mmol), N-(3-methoxypropyl)-N',N'-dimethyl-ethylenediamine (0.10 g, 0.62 mmol) obtained in Reference Example 10, 1-hydroxybenzotriazole (0.072 g, 0.47 mmol), N-methylmorpholine (0.10 mL, 1.2 mmol) and N,N-dimethylformamide (1.0 mL).

Please amend the paragraph starting at page 211, line 28 and ending at page 212, line 1 to read as follows.

In a manner similar to that in Example 10, Step 1, Compound 141 (0.087 g, 56%) was obtained from ~~2-ethyl-3,5-dihydroxy-6-(3,4-dimethoxybenzoyl)phenylacetic acid~~ 2-(3,4-dimethoxybenzoyl)-6-ethyl-3,5-dihydroxyphenyl acetic acid (0.11 g, 0.31 mmol) obtained in Example 40, Step 1, using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.17 g, 0.86 mol), N-(3-methoxypropyl)-N',N'-dimethyl-ethylenediamine (0.18 g, 1.15 mmol) obtained in Reference Example 10, 1-hydroxybenzotriazole (0.13 g, 0.86 mmol), N-methylmorpholine (0.10 mL, 1.2 mmol) and N,N-dimethylformamide (2.0 mL).

Please amend the paragraph starting at page 214, line 32 and ending at page 215, line 2 to read as follows.

In a manner similar to that in Example 88, Step 1, methyl 2-(3,4-difluorobenzoyl)-6-ethyl-3,5-dihydroxy-phenylacetate (1.5 g, 28%) was obtained from methyl 2-ethyl-3,5-dihydroxyphenylacetate (3.1 g, 15 mmol) obtained in Example 7, Step 1, Step 2, using 3,4-difluorobenzoyl chloride (2.6 g, 15 mmol) and boron trifluoride diethyl etherate (20 mL).

Please amend the paragraph at page 223, lines 23-30 to read as follows.

In a manner similar to that in Example 10, Step 1, Compound 151 (~~0.60 mg, 46%~~) (0.60 g, 46%) was obtained from 2-ethyl-3,5-dihydroxy-6-(3-thienylcarbonyl)phenylacetic acid (1.0 g, 3.3 mmol) obtained in Example 73, Step 3, using

1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (1.5 g, 7.8 mmol), 2-(2-methoxyethylamino)ethanol (1.6 g, 13 mmol) obtained in Reference Example 1 and N,N-dimethylformamide (7.0 mL).

Please amend the paragraph at page 226, lines 15-23 to read as follows.

In a manner similar to that in Example 10, Step 1, Compound 154 (67 mg, 42%) was obtained from 2-ethyl-3,5-dihydroxy-6-(3-thienylcarbonyl)phenylacetic acid (0.10 g, 0.33 mmol) obtained in Example 73, Step 3, using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (~~0.12 g, 0.76 mol~~, (0.12 g, 0.76 mmol), 1-(2-cyanophenyl)piperazin-2-one hydrochloride (0.17 g, 1.5 mmol) obtained by a method similar to the method described in Tetrahedron Lett., 1998, Vol. 39, p. 7459-7462 and N,N-dimethylformamide (1.0 mL).

Please amend the paragraph at page 227, lines 1-8 to read as follows.

In a manner similar to that in Example 10, Step 1, Compound 155 (44 mg, 30%) was obtained from 2-ethyl-3,5-dihydroxy-6-(3-thienylcarbonyl)phenylacetic acid (0.11 g, 0.36 mmol) obtained in Example 73, Step 3, using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (~~0.16 g, 0.76 mol~~, (0.16 g, 0.76 mmol), 4-piperidinemethanol (0.17 g, 1.4 mmol), 1-hydroxybenzotriazole hydrate (0.14 g, 0.89 mmol) and N,N-dimethylformamide (1.0 mL).

Please amend the paragraphs at page 227, lines 23-25 to read as follows.

Synthesis of 2-[2-ethyl-6-(3-furylcarbonyl)-3,5-dihydroxy-phenyl]-N,N-bis(2-methoxyethyl)acetamide (Compound 156)

(Step 1)

Please amend the paragraphs at page 230, lines 1-10 to read as follows.

(Step 1)

In a manner similar to that in Example 10, Step 2, Compound 158 (64 mg, 41%) was obtained from 2-(1,3-benzodioxol-5-yl)-6-ethyl-3,5-dihydroxyphenylacetic acid (120 mg, 0.35 mmol) obtained in Example 156, Step 3, using 1-hydroxybenzotriazole hydrate (80 mg, 0.52 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (100 mg, 0.52 mmol), 2-(2-methoxyethylamino)ethanol (200 mg, 1.7 mmol) obtained in Reference Example 1 and N,N-dimethylformamide (4 mL).

Please amend the paragraph starting at page 230, line 36 and ending at page 231, line 3 to read as follows.

In a manner similar to that in Reference Example 2, Example 1, 3-(2-methoxyethylamino)propanol (4.5 g, 43%) was obtained from 2-methoxyethylamine (21 mL, 0.24 mol), using 3-chloropropanol (6.6 mL, 0.079 mol) and water (3.0 mL).

Please amend the paragraph at page 235, lines 22-25 to read as follows.

¹H-NMR (CDCl₃, 270 MHz) δ (ppm): 7.97 (m, 1H), 7.66-7.60 (m, 3H), 6.45 (br.s, 1H), (brs, 1H), 6.27-6.22 (m, 2H), 4.66 (s, 2H), 4.54 (br.s, 1H), (brs, 1H), 3.86-3.79 (m, 2H), 3.58-3.45 (m, 4H), 1.87-1.51 (m, 6H)

Please amend the paragraph at page 236, line 33 to read as follows.

Synthesis of 4-(methylsulfonyl)piperidine hydrochloride

Please amend the paragraph at page 238, lines 19-25 to read as follows.

tert-Butyl 4-(methylsulfonyl)piperidine-1-carboxylate(2.4 g, 9.0 mmol) obtained in Reference Example 12, Step 3 was dissolved in ethyl acetate (16 mL), and a 4.0 mol/L solution of hydrogen chloride in dioxane (12 mL) was added thereto, followed by stirring for 3 hours. The precipitated solid was filtered to obtain 4-(methylsulfonyl)piperidine hydrochloride (1.4 g, 76%).